Does Creatine Supplementation Hinder Exercise Heat Tolerance or Hydration Status? A Systematic Review With Meta-Analyses

Rebecca M. Lopez, MS, ATC; Douglas J. Casa, PhD, ATC, FNATA, FACSM; Brendon P. McDermott, MS, ATC; Matthew S. Ganio, MS; Lawrence E. Armstrong, PhD, FACSM; Carl M. Maresh, PhD, FACSM

University of Connecticut, Storrs, CT

Objective: To critically assess original research addressing the effect of creatine supplementation on exercise heat tolerance and hydration status.

Data Sources: We searched the electronic databases PubMed, Scopus, Web of Science, SPORTDiscus, and Rehabilitation & Physical Medicine, without date limitations, for the following key words: creatine, exercise, thermoregulation, dehydration, hyperthermia, heat tolerance, exertional heat illnesses, and renal function. Our goal was to identify randomized clinical trials investigating the effect of creatine supplementation on hydration status and thermoregulation. Citations from related articles also were identified and retrieved.

Data Synthesis: Original research was reviewed using the Physiotherapy Evidence Database (PEDro) Scale. One author initially screened all articles. Fifteen of 95 articles examined the effects of creatine on thermoregulation or hydration status (or both). Two independent reviewers then reviewed these articles. Ten studies were selected on the basis of inclusion and exclusion criteria. The PEDro scores for the 10 studies ranged from 7 to 10 points (maximum possible score = 10 points).

Conclusions: No evidence supports the concept that creatine supplementation either hinders the body’s ability to dissipate heat or negatively affects the athlete’s body fluid balance. Controlled experimental trials of athletes exercising in the heat resulted in no adverse effects from creatine supplementation at recommended dosages.

Key Words: thermoregulation, dehydration, hypohydration, exertional heat illness, renal function

Key Points

- When recommended amounts were consumed, creatine supplementation did not appear to hinder the body’s ability to dissipate heat or negatively affect body fluid balance.
- Future researchers should evaluate the use of creatine during longer supplementation periods, exercise bouts that simulate games and practices, and more controlled field studies.

Many athletes have turned to nutritional supplements marketed as ergogenic aids to maximize athletic performance. Creatine is a naturally occurring element in the diet; it is also synthesized within the body, primarily by the liver. As a dietary supplement, creatine monohydrate is believed to enhance the resynthesis of adenosine triphosphate and to improve performance in short bouts of exercise. Creatine supplementation has been used by athletes for nearly 20 years, but speculation remains regarding its efficacy, as well as its potential side effects.

When creatine first gained media attention, many adverse events were attributed to its use, including the deaths of 3 National Collegiate Athletic Association wrestlers in 1997. Authors from several media reports on these fatalities and scientific review papers speculated on the possibility that creatine was a key factor leading to death. However, autopsy results determined that exertional heat stroke, not creatine, was responsible for these deaths. Creatine has also been implicated as possibly contributing to the deaths of several football players in recent years, but this suspicion has never been confirmed. Speculation that creatine may have influenced exertional heat stroke has resulted in an examination of its role in exercise heat intolerance.

Aside from the aforementioned media reports on creatine, most anecdotal reports of side effects have described muscle cramping or gastrointestinal distress. Other side effects potentially linked to creatine use include but are not limited to renal damage, susceptibility to muscle strains or cramps, and impairment of thermoregulation. The main concern involves its potential impairment of exercise heat tolerance and hydration status. These anecdotal reports, however, were never supported by clinical evidence.

After the media reports in the late 1990s, the American College of Sports Medicine sponsored a roundtable discussion entitled “The Physiological and Health Effects of Oral Creatine Supplementation.” Roundtable participants advised athletes to avoid creatine supplementation if they were “wishing to control weight” or “subjected to strenuous exercise and/or hot environments.” They also recommended avoiding high dosages of creatine “during periods of increased thermal stress, such as sports activities performed under high ambient temperature/humidity.
conditions.” These recommendations stemmed from the premise that supplementing with creatine can lead to a potentially impaired thermoregulation and altered fluid balance. To our knowledge, however, no scientific evidence existed at that time to support or refute these statements or any of the anecdotally reported side effects.

Theoretically, creatine uptake by the muscles results in an increase in fluid volume within skeletal muscle cells. Whether this increase helps, hinders, or does not influence thermoregulation has not been determined (Figure 1). Yet as a result of anecdotal reports and precautions regarding the potential detrimental effects of creatine supplementation, various researchers investigated the effects of creatine on hydration status and thermoregulation. The studies varied in methods, such as creatine dosages, exercise protocols, and ambient temperatures, making it difficult for a clinician to determine the best evidence-based clinical practice regarding creatine supplementation for

Figure 1. Does creatine hinder or help? Hypothetical considerations for influence of creatine on hydration status during rest and exercise in the heat. ECF indicates extracellular fluid.
athletes. Therefore, the purpose of our systematic review was to assess the evidence regarding the influence of creatine supplementation on exercise heat tolerance and hydration status.

METHODS

Data Sources

We searched the following electronic databases with no date limitations: PubMed, Scopus or Web of Science, SPORTDiscus, and Rehabilitation & Physical Medicine. These databases were searched in April 2007 using the following key words: creatine, exercise, thermoregulation, dehydration, hyperthermia, heat tolerance, exertional heat illnesses, and renal function. The search included human studies in English and Spanish but excluded articles pertaining to surgery and alcoholism.

Research articles pertaining to the effects of creatine supplementation on hydration status and thermoregulation were identified. All controlled clinical trials were initially examined. References from these articles and references from past review articles were then cross-referenced to identify additional articles for possible inclusion. Inclusion criteria were experimental studies with washout periods of 28 or more days (crossover experimental design) and dependent variable(s) of hydration or thermoregulatory status with the purpose related to evaluating the effects of creatine supplementation on hydration or thermoregulation or both. Only studies with physically active male or female participants were included. Articles were excluded if they were reviews, addressed nonactive individuals, or used a creatine dosage that was less than 2 g · d\(^{-1}\) or that was administered for fewer than 5 days. Articles receiving a score of less than 7 on the Physiotherapy Evidence Database Scale (PEDro) Scale\(^{23}\) (Table 1) were also excluded, because a lower score indicated that internal validity or blinding of participants was lacking.

Quality Assessment

Authors of 15 of the 95 identified articles examined the effects of creatine on thermoregulatory measures or hydration measures or both. After meeting our inclusion criteria, these 15 articles were reviewed by 2 independent reviewers using the PEDro Scale\(^{23}\) (Figure 2). This scale consists of a checklist to determine 2 aspects of a study’s quality: (1) the internal validity of the trial and (2) whether

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Table 1. Physiotherapy Evidence Database (PEDro) Scale\(^{23}\)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points Awarded</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Eligibility criteria were specified (no points awarded)</td>
<td>1</td>
</tr>
<tr>
<td>2. Subjects were randomly allocated to groups or order in which treatments received</td>
<td>1</td>
</tr>
<tr>
<td>3. Allocation was concealed</td>
<td>1</td>
</tr>
<tr>
<td>4. The groups were similar at baseline regarding the most important prognostic indicators</td>
<td>1</td>
</tr>
<tr>
<td>5. There was blinding of all subjects</td>
<td>1</td>
</tr>
<tr>
<td>6. There was blinding of all therapists who administered the therapy</td>
<td>1</td>
</tr>
<tr>
<td>7. There was blinding of all assessors who measured at least one key outcome</td>
<td>1</td>
</tr>
<tr>
<td>8. Measures of at least 1 key outcome were obtained from more than 85% of the subjects initially allocated to groups</td>
<td>1</td>
</tr>
<tr>
<td>9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least 1 key outcome were analyzed by “intention to treat.”</td>
<td>1</td>
</tr>
<tr>
<td>10. The result of between-groups statistical comparisons are reported for a least 1 key outcome</td>
<td>1</td>
</tr>
<tr>
<td>11. The study provides both point measures and measures of variability for at least 1 key outcome</td>
<td>1</td>
</tr>
</tbody>
</table>

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Figure 2. Criteria for selection of articles for review.
Table 2. Studies Investigating the Influence of Creatine on Hydration Status and Exercise Heat Tolerance

<table>
<thead>
<tr>
<th>Study</th>
<th>Methods</th>
<th>Participants</th>
<th>Participant Characteristics</th>
<th>Exercise Protocol and Environment (Temperature, Relative Humidity)</th>
<th>Dosage</th>
<th>Body Temperature Differences (Creatine Versus No Creatine)</th>
<th>Difference in Hydration Variables</th>
<th>PEDro Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wright et al(^\text{22}) (2007)</td>
<td>Randomized, single blind, crossover</td>
<td>n = 10</td>
<td>Physically active, heat-acclimatized men</td>
<td>Cycle ergometer, 30-min warm-up, 6 × 10-s maximal sprints (35°C, 60%)</td>
<td>Creatine: 20 g·d(^{-1}) for 6 d; placebo: 20 g·d(^{-1}) maltodextrin</td>
<td>No differences in (T_e)</td>
<td>↑ BM with creatine (1.30 kg), sweat losses not different</td>
<td>7</td>
</tr>
<tr>
<td>Easton et al(^\text{8}) (2007)</td>
<td>Randomized, double blind</td>
<td>Creatine, n = 12; placebo, n = 12</td>
<td>Endurance-trained men</td>
<td>Cycle ergometer, 40 min, 63% maximal work rate (30°C, 70%)</td>
<td>Two 7-d, twice-daily regimens: Creatine: 10 g; placebo: 85 g glucose, plus 1 g·kg(^{-1}) glycerol or placebo</td>
<td>↓ (T_e) Postexercise versus pre-exercise with creatine ((P &lt; .01))</td>
<td>Creatine: ↑ BM, TBW, ICW; no difference in sweat rates</td>
<td>10</td>
</tr>
<tr>
<td>Branch et al(^\text{7}) (2007)</td>
<td>Randomized, double blind, crossover</td>
<td>n = 7</td>
<td>Competitive male cyclists and triathletes</td>
<td>Cycle ergometer, three 1-h sessions, approximately 66% (V_{\text{O}2\text{max}}) (38°C, 33%)</td>
<td>Creatine: 20 g·d(^{-1}) for 5 d; placebo: 20 g·d(^{-1}) dextrose; ≥28-d washout</td>
<td>Tympatic temperature not a valid measure for exercising individuals</td>
<td>No difference in pre-exercise BM or postexercise % dehydration</td>
<td>10</td>
</tr>
<tr>
<td>Watson et al(^\text{16}) (2006)</td>
<td>Randomized, double blind, crossover</td>
<td>n = 12</td>
<td>Non–heat-acclimated, active males</td>
<td>120 min of alternating treadmill, cycling, approximately 37.1% (V_{\text{O}2\text{max}}) (33.5°C, 41%)</td>
<td>Creatine: 21.6 g monohydrate, 7 d; placebo: 21.6 g, 7 d; 48 ± 10-d washout</td>
<td>No differences in (T_e)</td>
<td>Creatine: ↑ BM (0.88 kg), days 1–7; urine color and creatine concentration greater pre-exercise; urinary specific gravity higher pre-exercise, postexercise; placebo: ↑ plasma volume</td>
<td>10</td>
</tr>
<tr>
<td>Weiss and Powers(^\text{17}) (2006)</td>
<td>Randomized, double blind</td>
<td>Creatine, n = 12; placebo, n = 12</td>
<td>Aerobically trained males</td>
<td>Stationary cycling, 60 min, 70% maximum heart rate (37°C)</td>
<td>Creatine: 25 g·d(^{-1}) for 5 d; placebo: isocaloic capsules</td>
<td>No differences in (T_{\text{GI}})</td>
<td>Creatine: ↑ TBW, ICW, ECW; sweat losses not different</td>
<td>10</td>
</tr>
<tr>
<td>Mendel et al(^\text{22}) (2005)</td>
<td>Double blind</td>
<td>Creatine, n = 8; placebo, n = 8</td>
<td>15 Untrained but recreationally active males, 1 female</td>
<td>Cycle ergometer, 40 min, 55% (V_{\text{O}2\text{max}}) (39°C)</td>
<td>Creatine: 20 g·d(^{-1}) for 5 d; placebo: 10 g·d(^{-1}) powdered cellulose for 5 d</td>
<td>With creatine, (T_{\text{re}}) lower than with placebo at 40 min but not significant</td>
<td>Creatine: ↑ BM (1.4 kg) presuppplementation to postsuppplementation</td>
<td>9</td>
</tr>
<tr>
<td>Kiduff et al(^\text{11}) (2004)</td>
<td>Randomized, double blind</td>
<td>Creatine, n = 11; placebo, n = 10</td>
<td>Endurance-trained, non–heat-acclimated males</td>
<td>2 Cycle ergometer tests to exhaustion, 47 min, 63% (V_{\text{O}2\text{max}}) (30.3°C)</td>
<td>Creatine: 20 g·d(^{-1}) for 7 d; placebo: 160 g·d(^{-1}) glucose for 7 d (polymer)</td>
<td>(T_{\text{re}}) lower at 35 min, 40 min, and exhaustion postsuppplementation versus presuppplementation supplementation ((P &lt; .01))</td>
<td>Creatine: ↑ BM, TBW, ICW; ↓ sweat rate postsuppplementation</td>
<td>10</td>
</tr>
<tr>
<td>Study</td>
<td>Methods</td>
<td>Participants</td>
<td>Exercise Protocol and Environment (Temperature, Relative Humidity)</td>
<td>Dosage</td>
<td>Body Temperature Differences (Creatine Versus No Creatine)</td>
<td>Difference in Hydration Variables</td>
<td>PEDro Score</td>
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<tr>
<td>Powers et al (2003)</td>
<td>Randomized, double blind</td>
<td>Creatine, n = 16; placebo, n = 16</td>
<td>Resistance-trained males and females</td>
<td>Maintained their resistance-training programs, kept log of repetitions, sets, resistance</td>
<td>Creatine: 25 g·d⁻¹ for 7 d, then 5 g·d⁻¹ for 21 d; placebo: sucrose</td>
<td>No thermoregulatory measures reported</td>
<td>Creatine: greater urinary creatine; women: greater urinary creatine, 7 and 28 d; ↑ BM presupplementation to postsupplementation; greater TBW than placebo at 7 and 28 d</td>
<td>10</td>
</tr>
<tr>
<td>Kern et al (2001)</td>
<td>Randomized, double blind</td>
<td>Creatine, n = 10; placebo, n = 10</td>
<td>Healthy, college-aged, moderately to highly active males</td>
<td>Cycle ergometer, 60 min, 60% VO₂max (37°C, 25%)</td>
<td>Creatine: 21 g·d⁻¹ for 5 d, then 10 g·d⁻¹ for 23 d; placebo: Phosphagen HP matrix minus creatine</td>
<td>Creatine: Tₑ 0.37°C lower than presupplementation, creatine: Tₑ 0.20°C lower than placebo (P = .022)</td>
<td>Creatine: ↑ BM, TBW</td>
<td>10</td>
</tr>
<tr>
<td>Volek et al (2001)</td>
<td>Randomized, double blind</td>
<td>Creatine, n = 10; placebo, n = 10</td>
<td>Healthy men</td>
<td>Cycle ergometer, 30 min, continuous 10-s maximum sprints, 60%—70% VO₂max (37°C, 80%)</td>
<td>Creatine: 0.3 g·kg⁻¹·d⁻¹ for 7 d; placebo: powdered cellulose</td>
<td>No differences in Tₑ</td>
<td>Creatine: ↑ BM (0.75 kg), TBW presupplementation to postsupplementation, serum creatinine after 1 wk</td>
<td>10</td>
</tr>
</tbody>
</table>

Abbreviations: BM, body mass; ECW, extracellular water; ICW, intracellular water; TBW, total body water; Tₑ, gastrointestinal temperature; Tₑ, rectal temperature.
information is sufficient to interpret the results.\textsuperscript{23} The PEDro Scale contains 11 items, 10 of which contribute to the score (Table 1). Each yes response is worth 1 point, whereas a no response is worth 0 points, for a maximum possible of 10 points. The PEDro Scale or variations of this scale have been used in other systematic reviews as a means of determining the quality of controlled trials.\textsuperscript{24–27}

The PEDro scores for the 15 articles ranged from 3 to 10 points. Scores were recorded, and the 2 investigators met to review any discrepancies. The interrater agreement for the PEDro scores of the 2 investigators was initially moderate\textsuperscript{28} ($\kappa = 0.530$); however, after the investigators reviewed the scores, they reached full consensus ($\kappa = 1.00$). Five articles were excluded because of their low PEDro scores (less than 7 of 10 points), resulting from lack of participant blinding or lack of focus on thermoregulatory measures. The PEDro scores for the 10 selected articles ranged from 7 to 10 points.

**Statistical Analysis**

We quantified the effect of creatine ingestion on thermoregulation by performing a meta-analysis of the body temperature data using RevMan software (version 5.0; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). RevMan was used for calculating the $\chi^2$ distribution to determine heterogeneity and to test for overall effect, weighted averages, mean differences, effect estimates, and 95\% confidence intervals. Weighted percentages were based on the studies’ sample sizes. We used SPSS software (version 16.0; SPSS Inc, Chicago, IL) to determine interrater agreement for the PEDro scores.

**RESULTS**

**Data Synthesis**

The focus of our search was to determine what differences, if any, were present between participants supplementing with creatine and those supplementing with placebo with regard to the following dependent variables: a valid body temperature assessment (eg, rectal [$T_{re}$] temperature or gastrointestinal [$T_{GI}$]), body mass, total body water (TBW), intracellular water (ICW), extracellular water (ECW), heart rate, and urinary and plasma measures (Table 2).

Wright et al\textsuperscript{22} examined the effects of 6 days of creatine loading on thermoregulation in a hot, humid environment (35\°C, 60\% relative humidity) during a sprint performance on a cycle ergometer. Creatine loading resulted in increased body mass (+1.30 kg) compared with the placebo condition ($P < .05$). Although the exercise bout resulted in increased core temperature, loss of body water, and a change in plasma volume, these measures were not different between the creatine and placebo conditions.\textsuperscript{22}

Easton et al\textsuperscript{8} investigated the effects of combined creatine and glycerol supplementation on responses to exercise in the heat. Although these authors looked at combining creatine with glycerol supplementation, we focused on the interaction effects between the creatine and placebo conditions only. Body mass, TBW, ICW, and ECW were increased compared with placebo. However, no differences were noted in total sweat losses between the conditions. After supplementation, $T_{re}$ was lower during exercise in the creatine condition ($P < .01$).

Branch et al\textsuperscript{7} examined the effects of creatine supplementation on competitive male cyclists and triathletes while cycling in the heat (38.7\°C). No differences were seen between the creatine and placebo groups for heart rate or rating of perceived exertion (RPE). Postexercise, plasma volume decreased in the baseline and placebo conditions compared with the creatine condition ($P = .013$). Fluid consumed, exercise-induced dehydration, and pre-exercise and postexercise body mass were not different between conditions. Branch et al\textsuperscript{7} used tympanic temperature, which is not a valid measure of body temperature.\textsuperscript{29}

Watson et al\textsuperscript{16} examined the effects of 1 week of creatine supplementation on hydration status, thermoregulation, and incidence of heat illness in dehydrated men exercising in a hot environment. Body mass and sweat losses during exercise were not different between conditions; however, an interaction was demonstrated in the body mass change from day 1 to day 7 of creatine supplementation ($P = .015$). Urine specific gravity was higher for the creatine group before ($P = .030$) dehydration and pre-exercise ($P = .004$) and postexercise ($P = .009$) heat tolerance test. Compared with placebo, plasma osmolality was higher during creatine supplementation before ($P = .032$) and after ($P = .015$) dehydration, as well as 20 minutes into recovery ($P = .008$).

The investigation of Weiss and Powers\textsuperscript{17} consisted of a 5-day supplementation period followed by a 60-minute bout of exercise in a warm environment. Aerobically trained males exhibited no differences in heart rate or sweat losses. Group $\times$ day interactions were observed for TBW ($P = .004$), ICW ($P = .046$), and ECW ($P = .005$), with the creatine group experiencing an increase in each of the 3 body water volumes. No $T_{GI}$ differences were found between groups ($P = .87$).

Mendel et al\textsuperscript{12} investigated the effects of creatine on thermoregulatory responses during exercise in a hot environment (39\°C). Five days of creatine supplementation resulted in a 1.4-kg increase in body mass postsupplementation ($P = .013$). Although not different, $T_{re}$ was lower at 40 minutes of exercise for the creatine group.

Kilduff et al\textsuperscript{11} examined the effects of creatine on thermoregulatory, cardiovascular, and metabolic responses during exercise in the heat in endurance-trained males. Body mass, TBW, and ICW increased in the creatine group. After supplementation, heart rate was lower in the creatine group from 35 minutes of exercise until exhaustion ($P = .044$). Compared with presupplementation, postsupplementation $T_{re}$ was lower at 35 minutes and 40 minutes and at exhaustion ($P = .012$). Heart rate also was reduced after creatine supplementation (32.3 $\pm$ 7.0 mL $\cdot$ min$^{-1}$ versus 28.2 $\pm$ 3.9 mL $\cdot$ min$^{-1}$, $P = .02$).

Powers et al\textsuperscript{13} examined the effects of 28 days of creatine supplementation on fluid distribution. The creatine group had greater body mass from presupplementation to day 28 ($P = .44$). Compared with placebo, the creatine group had greater TBW volume on days 7 and 28 ($P = .027$), with no differences in ECW and ICW ($P = .366$).

Kern et al\textsuperscript{10} examined hydration status and indicators of heat tolerance after 28 days of creatine supplementation. In the creatine condition, body mass ($P = .034$) and TBW increased ($P = .050$). Compared with presupplementation,
postsupplementation $T_{re}$ for the creatine group was 0.37°C lower; compared with the placebo group, postsupplementation $T_{re}$ was 0.20°C lower ($P = .022$ for differences from presupplementation to postsupplementation between the creatine and placebo groups). No differences were noted in heart rate responses to exercise in the heat between conditions.

Volek et al$^{15}$ provided participants with 7 days of creatine supplementation. Body mass increased 1 week postsupplementation (0.75 kg, $P = .05$). Body mass losses and sweat rate during 35 minutes of exercise in the heat (38°C) were not different between groups ($P > .05$). Plasma volume changes, $T_{re}$, heart rate, and RPE were not different between groups ($P > .05$). Urinary volumes over 24 hours tended to be greater for the creatine group, but were only significantly greater than placebo on day 3 of supplementation ($P < .05$).

### Meta-Analysis Test Outcomes

The test for heterogeneity was not significant: $\chi^2_7 = 10.9$, $P = .14$. Using a fixed-effects inverse variance analysis model, the test for overall effect was not significant ($Z = 0.56, P = .57$). With the 8 studies ($n = 167$) included in the meta-analysis, the effect estimate $= 0.03$ (95% confidence interval $= -0.07, 0.13$). Weighted averages, mean differences, and 95% confidence intervals are reported in Table 3 and Figure 3.

### DISCUSSION

Despite anecdotal reports of creatine side effects in athletes exercising in the heat, none of the 10 studies$^{7,8,10–13,15–17,22}$ showed detrimental in thermoregulatory or hydration variables, including body temperature regulation, percentage of dehydration, urinary hydration measures, plasma volume, or sweat losses (Table 2).

### Participant Characteristics, Exercise Protocols, Environmental Conditions, and Creatine Dosing

The similarities and differences among participant characteristics, exercise protocols, and environmental conditions are illustrated in Table 2. Variations in methods did not affect the influence of creatine supplementation.

The amount of creatine consumed was similar among trials (20–25 g · d$^{-1}$), whereas the supplementation duration varied (5–28 days). Despite variations in dosages, the

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**Table 3. Differences in Body Temperature (°C) Between Creatine Versus No Creatinea**

<table>
<thead>
<tr>
<th>Study</th>
<th>Creatine Mean ± SD</th>
<th>Creatine Total</th>
<th>Placebo Mean ± SD</th>
<th>Placebo Total</th>
<th>Mean Difference</th>
<th>Weight, %</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easton et al (2007)$^b$</td>
<td>39.20 ± 0.50</td>
<td>12</td>
<td>39.05 ± 0.50</td>
<td>11</td>
<td>0.20</td>
<td>6.4</td>
<td>0.15 [−0.26, 0.56]</td>
</tr>
<tr>
<td>Kern et al (2001)$^{10}$</td>
<td>38.25 ± 0.35</td>
<td>9</td>
<td>38.45 ± 0.35</td>
<td>10</td>
<td>-0.05</td>
<td>10.9</td>
<td>-0.20 [−0.52, 0.12]</td>
</tr>
<tr>
<td>Kilduff et al (2004)$^{11}$</td>
<td>39.25 ± 0.40</td>
<td>11</td>
<td>39.50 ± 0.55</td>
<td>10</td>
<td>0.27</td>
<td>6.3</td>
<td>-0.25 [−0.66, 0.16]</td>
</tr>
<tr>
<td>Mendel et al (2005)$^{12}$</td>
<td>38.10 ± 0.40</td>
<td>8</td>
<td>38.40 ± 0.30</td>
<td>8</td>
<td>0.20</td>
<td>9.0</td>
<td>-0.30 [−0.85, 0.05]</td>
</tr>
<tr>
<td>Volek et al (2001)$^{11}$</td>
<td>38.57 ± 0.07</td>
<td>10</td>
<td>38.39 ± 0.26</td>
<td>10</td>
<td>0.56</td>
<td>38.7</td>
<td>0.18 [0.01, 0.35]</td>
</tr>
<tr>
<td>Watson et al (2006)$^{16}$</td>
<td>39.40 ± 0.40</td>
<td>12</td>
<td>39.30 ± 0.40</td>
<td>12</td>
<td>0.30</td>
<td>10.5</td>
<td>0.10 [−0.22, 0.42]</td>
</tr>
<tr>
<td>Weiss and Powers (2006)$^{17}$</td>
<td>38.44 ± 0.42</td>
<td>12</td>
<td>38.42 ± 0.29</td>
<td>12</td>
<td>0.36</td>
<td>12.9</td>
<td>0.02 [−0.27, 0.31]</td>
</tr>
<tr>
<td>Wright et al (2007)$^{22}$</td>
<td>38.07 ± 0.47</td>
<td>10</td>
<td>38.04 ± 0.56</td>
<td>10</td>
<td>0.35</td>
<td>5.3</td>
<td>0.03 [−0.42, 0.48]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>84</td>
<td></td>
<td>83</td>
<td></td>
<td></td>
<td>100.0</td>
<td>0.03 [−0.07, 0.13]</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; IV, inverse variance; SD, standard deviation.

*a Based on a fixed-effects model. No relationship was noted between treatment effects and body temperature (°C), as shown by 95% CI. Weighted percentages were based on sample sizes. Effect estimate $= 0.03$ (95% CI $= −0.07, 0.13$). Heterogeneity: $\chi^2 = 10.90$, degrees of freedom $= 7$ ($P = .14$); $I^2 = 36\%$. Test for overall effect: $Z = 0.56$ ($P = .57$).
results of the 10 studies were similar with regard to changes in body mass and body temperature. None of the studies included in this review (Table 2) involved creatine supplementation for longer than 28 days. One of the greatest concerns about creatine use is that few authors have examined its long-term effects. Although Kreider et al\textsuperscript{20} examined the effects of creatine dosages over a 21-month period, they did not focus on markers of hydration or thermoregulation. Further studies involving long-term creatine supplementation and its effects on hydration and thermoregulation are necessary to determine possible adverse effects.

**Effects on Body Temperature**

Six of the 10 groups reported no differences between creatine and placebo in body temperature while exercising in the heat (Table 3). However, one group\textsuperscript{29} measured tympanic temperature, which was mentioned as a limitation of the study because it does not validly represent central body temperature in exercising individuals. In 3 of the 10 studies,\textsuperscript{8,10,11} $T_r$ was lower after creatine supplementation. Although the finding was not significant, one group\textsuperscript{12} also reported lower $T_r$ for creatine (compared with placebo) after 40 minutes of exercise. The decreased body temperature in these studies could be attributed to factors such as increases in body mass and TBW, because the findings were similar (Table 2), but how an increase in these measures would attenuate a rise in body temperature is unclear. None of these authors\textsuperscript{8,10,11} found an increase in sweat rate, which might have improved thermoregulation.

These results indicate that creatine supplementation was not a detriment to thermoregulation while exercising in the heat when supplementation took place over the course of 5 to 28 days. Many researchers\textsuperscript{1–4,6} have questioned whether creatine supplementation hinders thermoregulation and predisposes an athlete to exertional heat stroke (Figure 1). However, this review demonstrates no differences in body temperature with creatine supplementation, and some groups\textsuperscript{8,10,11} even showed that creatine attenuated the rise in body temperature during exercise in the heat. During severe dehydration, the osmotic influence of creatine could be trumped by hyperosmotic extracellular fluid (ECF), resulting in excess fluid entering the ECF and possibly decreasing the strain on thermoregulation, as depicted in Figure 1.

**Effects on Hydration Measures**

Previous authors\textsuperscript{21} have found that acute creatine ingestion elevated TBW and ICF but had no effect on ECW after 3 days of supplementation. These results are similar to those of some of the reviewed studies, in which authors reported increases in TBW,\textsuperscript{8,10,11,13,15,17} increases in ICW and ECW,\textsuperscript{8,17} and increases in ICW but not ECW.\textsuperscript{11} Although other researchers found no differences in sweat rate with creatine supplementation,\textsuperscript{17,22} only one group\textsuperscript{11} noted a decrease in sweat rate with creatine supplementation.

The most common effect of creatine supplementation found in the literature has been a change in body mass, but this finding does not seem to alter exercise sweat rates.\textsuperscript{7,8,14,17,22} Investigators on 9 of the 10 studies in this review reported an increase in body mass as a result of creatine supplementation.\textsuperscript{8,10,13,15–17,22} Changes in total body mass could be detrimental in sports that depend on specific body weights (ie, wrestling, gymnastics). More importantly, changes in body mass and TBW have been the cause of reservations regarding thermoregulation\textsuperscript{1} (Figure 1). Several authors\textsuperscript{8,11,17,21} have found increases in ICW as a result of creatine supplementation; none of these resulted in signs or symptoms of heat illness or impaired thermoregulation. Further, it has been suggested\textsuperscript{8,10,11} that these increases in TBW and ICW might actually assist in maintaining or improving thermoregulation. Results from earlier researchers\textsuperscript{21} noted osmotic fluid shifts within as few as 3 days of creatine supplementation. However, Casa et al\textsuperscript{30} found that after 10 days of supplementation, creatine did not alter fluid distribution or promote an osmotic fluid shift between fluid compartments. Furthermore, authors\textsuperscript{18} investigating National Collegiate Athletic Association Division I-A college football players found that the incidence of cramping or injury for creatine users was lower than or proportional to that of non–creatine users. The different TBW, ICW, and ECW changes can be attributed to variations in the amount and duration of creatine dosages as well as to differences in methods (Table 2). The variations in hydration outcome measures made it difficult to identify the influence of creatine supplementation on fluid balance; however, based on these studies, creatine does not seem to impair hydration status or thermoregulation. Furthermore, the findings from the objective approach used in this systematic review seem to reiterate the findings reported in a recent review on this topic.\textsuperscript{31}

**PEDro Scale**

We selected the PEDro Scale to assess the quality of relevant articles. The PEDro Scale is intended to identify controlled, unbiased experimental trials to ensure internal validity and to determine if the results of the research can be interpreted. One can conclude that the higher the PEDro score a study received, the better the study quality and the greater the likelihood that the results are a valid estimate of the truth.\textsuperscript{24} The scores we generated were relatively high in comparison with PEDro scores of other systematic reviews.\textsuperscript{24,27} This result could be attributed to (1) a recent increase in higher-quality, randomized, controlled trials in the areas of thermoregulation and hydration, as well as (2) 3 points in the scale reflecting blinding of participants. Authors of controlled studies\textsuperscript{24,27} in other systematic reviews may have not been able to blind their participants or researchers to the treatment given.

**CONCLUSIONS**

No substantial evidence currently exists showing that creatine supplementation hinders the body’s ability to dissipate heat or body fluid balance when appropriate doses are consumed. Controlled experimental trials of athletes exercising in the heat over a short period of time resulted in no adverse effects from creatine supplementation. Future researchers should include longer supplementation periods, exercise bouts that simulate a game or practice situation (ie, greater than 60 minutes in duration), and more controlled field studies.

As clinicians working with athletes on a daily basis, athletic trainers, other allied health professionals, and
physicians must ask themselves, “What underlies the anecdotal reports of adverse effects from creatine?” As clinicians, we should be asking how to connect experimental trials and real-life situations. Allied health professionals should use evidence-based medicine to determine clinical applications.

REFERENCES

The Influence of Nutritional Ergogenic Aids on Exercise Heat Tolerance and Hydration Status

Rebecca M. Lopez and Douglas J. Casa
Human Performance Laboratory, Department of Kinesiology, Neag School of Education, University of Connecticut, Storrs, Connecticut

LOPEZ, R.M. and D.J. CASA. The influence of nutritional ergogenic aids on exercise heat tolerance and hydration status. Curr. Sports Med. Rep., Vol. 8, No. 4, pp. 192–199, 2009. Exercise in the heat may predispose an athlete to an exertional heat illness. It is imperative to be knowledgeable on the influence of various nutritional supplements on exercise tolerance and hydration status. Because of the variety of nutritional ergogenic aids that are easily accessible to athletes, medical and health professionals must rely on empirical evidence when making conclusions about the efficacy of a supplement while not ignoring significant anecdotal reports that may resemble real-life situations more closely.

INTRODUCTION

The use of supplements to improve athletic performance has an extensive history by a wide range of competitive athletes. Along with the proposed ergogenic effects of numerous supplements, which are often not proven or are exaggerated greatly, there could be harmful and potentially fatal side effects. Many athletes have a “win at all costs” mentality and will choose to use a supplement regardless of the possible side effects. Furthermore, many of the side effects reported with supplements are anecdotal and have not been supported by scientific evidence.

Exercise in the heat can have added risks to athletes. Recent exertional heat stroke deaths have increased media attention to some supplements and their potential connection with exertional heat stroke (7,15). Unfortunately, some of these reports and recommendations on the use of supplements are speculative and not based on factual evidence or scientific research (7,55). As a result, athletes are misinformed on which supplements may predispose them to an exertional heat illness. They are unaware what preventative measures to take when exercising in the heat. It is imperative that medical professionals educating athletes are knowledgeable about the various performance enhancers and their possible effects on heat tolerance to be able to give sound recommendations to competitive athletes and other physically active populations. Randomized-controlled trials (6,17,22,26,28,52,56,57) have resulted in evidence-based recommendations regarding the use of ergogenic supplements. Therefore, the purpose of this article is to describe the influence of popular nutritional supplements on hydration status and thermoregulation.

CREATINE

Although creatine was first identified in 1835, creatine supplementation became increasingly popular in athletic populations in the 1990s (4). Creatine’s popularity stemmed from research demonstrating an increase in skeletal muscle phosphocreatine content and increased performance in some subjects (55). Creatine is a dietary element found in meat and fish; however, creatine also is synthesized by the body and can be found in skeletal muscle, heart muscle, and other organs (27). Many athletes supplement with creatine because it has been shown to increase muscle concentrations of total creatine and phosphocreatine (32). This increase in creatine and phosphocreatine potentially can act as a source of adenosine triphosphate in skeletal muscles, thereby increasing performance in short-duration, high-intensity bouts of exercise (55).

Initial reports on the efficacy and safety of creatine supplementation included warnings of possible long-term effects of creatine and anecdotal reports of increased risk of heat illness and muscle injury (Figure; Table 1). In the late ’90s, several media reports and scientific papers linked creatine to
several athletes’ deaths (7,55). As a result, many have speculated that individuals supplementing with creatine are at greater risk of heat illness when exercising in hot and/or humid environments. In 2000, the American College of Sports Medicine’s roundtable on creatine supplementation cautioned athletes on supplementing with creatine while exercising in the heat (55). However, there was no evidence at this time to support an increased risk of an exertional heat illness as a result of creatine supplementation. These anecdotal claims resulted in an increase in scientific studies investigating the relationship between creatine and hydration status and/or heat intolerance (12,14,20,26,29,30,41,48,51,56,57,59,61,62). A systematic review of the existing literature on the influence of creatine on thermoregulation and hydration status concluded that there is no evidence to support claims that creatine impedes heat tolerance or hydration status (35). As Table 2 illustrates, the systematic review failed to show significant differences in body temperature between the creatine and placebo groups while exercising in the heat.

The most common side effect from creatine supplementation is increased body mass as a result of water retention. This weight gain has been hypothesized to affect the body’s ability to thermoregulate by altering body fluid balance. Researchers investigating the effect of creatine on body fluid balance have had varying results. One study found that 10 d of creatine supplementation did not result in altered fluid distribution or promote an osmotic fluid shift between fluid compartments (14). Several studies found that supplementing with creatine increases total body water (20,29,30,48,56,59,61,62) and intracellular water (30,59,62), yet others have found increases in extracellular water as well (20,59). This increase in total body water is evident in subjects who have an increased body mass post-supplementation. However, this influence of a possible fluid shift has not had any detrimental effects on subjects’ ability to dissipate heat when exercising in the heat. Several studies have found that subjects supplementing with creatine had a lower heart rate and core body temperature (20,29,30) while exercising in the heat when compared with placebo. Also, subjects supplementing with creatine who already were dehydrated before exercising in the heat showed no signs of heat intolerance compared with placebo (57).

Researchers have concluded that both long-term and short-term creatine supplementation may have no effect or may even be advantageous for athletes exercising in the heat (12,14,20,23,29,30,35,41,57,59,61). The evidence from the recent increase in controlled studies does not support previous claims that creatine may hinder heat tolerance and/or
hydration status. In fact, some studies found that caffeine resulted in a lower body temperature than placebo when exercising in the heat (29,30,41). Although the rationale behind this has not been elucidated, perhaps the increased total body water seen with creatine supplementation results in improved thermoregulation. Therefore, there is a lack of evidence to support advising athletes who are supplementing with creatine to avoid exercise in the heat (35).

CAFFEINE

Caffeine, or 1,3,7-trimethylxanthine, is one of the most widely used drugs. Recently, there has been an increase in caffeine intake by athletes to improve athletic performance. Only low to moderate doses of caffeine (3–10 mg·kg\(^{-1}\)) are needed to bring about an ergogenic effect (18). Researchers have found that these nontoxic doses of caffeine improve athletic performance, particularly endurance exercise (18). Some evidence suggests that caffeine also may serve as an ergogenic aid in high-intensity bouts of exercise (18).

Although caffeine is a popular drug among general and athletic populations alike, caffeine often has been linked with dehydration and/or heat intolerance (Table 1). The theory behind this could be attributed to caffeine’s diuretic effect, the stimulation of the sympathetic nervous system, or an increase in resting metabolic rate (5). As a result, athletes sometimes are advised to abstain from caffeine while exercising, particularly in the heat. Recent studies have sought to determine whether there is evidence to support advising athletes to abstain from caffeine because of hydration and/or thermoregulatory impairments (6,17,19,21,22,42,52,54).

Studies have investigated the short- and long-term effects of various levels of caffeine ingestion on hydration status and thermoregulation in thermoneutral, warm, and hot conditions (Table 3). A study investigating the effects of acute caffeine ingestion on thermoregulation and body fluid balance during prolonged exercise in a thermoneutral environment found no adverse effects of caffeine on body fluid balance or thermoregulatory or metabolic responses (21). Following ingestion of 5 and 2.5 mg·kg\(^{-1}\) of caffeine at 2 and 0.5 h of exercise, respectively, there were no significant differences in final rectal temperature, total water loss, sweat rate, rise in rectal temperature, and percent change in plasma volume compared with placebo (21).

Similarly, another study examined the effects of 6 mg·kg\(^{-1}\) of caffeine before exercise in high ambient temperatures on hemodynamic and body temperature responses (54). This study found significant increases in lactate and heart rate during exercise as a result of caffeine; however, caffeine again had no effect on body temperature during exercise. Several other researchers have found similar results with acute caffeine intake having no adverse effects on fluid-electrolyte balance (42,52), sweat rate (22,52), urine osmolality (22,52), or thermoregulatory responses (22,42,52) compared with non-caffeinated sports drinks or placebo.

Although most studies have investigated the effects of acute or short-term caffeine ingestion, one study looking at the effects of long-term caffeine intake on hydration found little evidence to suggest that chronic caffeine intake may lead to dehydration or heat intolerance (6). Armstrong et al. examined the effects of three levels of caffeine consumption on fluid-electrolyte balance and renal function. Although this study supported previous findings that caffeine may act as a diuretic soon after consumption, urine volumes, serum osmolality, and all other hydration measures were similar among all treatment groups on all days (6). Until this study, little was known about the effects of chronic caffeine consumption greater than 24 h on hydration status. Across 11 d, changes in caffeine dosage had no significant effect on body mass or urinary indices (6). This study found no evidence to suggest that athletes consuming moderate amounts of caffeine (3–6 mg·kg\(^{-1}\)·d\(^{-1}\)) are at greater risk of hypohydration and/or heat intolerance while exercising (6 mg·kg\(^{-1}\)·d\(^{-1}\)) for a 70-kg individual is equivalent to the following intake per day: 4 cups of coffee (8 oz.), 10 cans of Coca-Cola (12 oz.), or 5 cans of Red Bull (8 oz.), for example. Furthermore, caffeine’s influence as a mild diuretic likely is negated when fluid status is compromised during exercise in the heat.

<table>
<thead>
<tr>
<th>Study</th>
<th>Creatine Group</th>
<th>Placebo Group</th>
<th>Mean Difference (Creatine–Placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean  SD  Participants</td>
<td>Mean  SD  Participants</td>
<td>Weighting Factor (95% Confidence Interval)</td>
</tr>
<tr>
<td>----------------</td>
<td>----------------</td>
<td>--------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Easton et al. (2007) (20)</td>
<td>39.2 0.5 12</td>
<td>39.05 0.5 11</td>
<td>6.40% 0.15 (0.026, 0.56)</td>
</tr>
<tr>
<td>Kern et al. (2001) (29)</td>
<td>38.25 0.35 9</td>
<td>38.45 0.35 10</td>
<td>10.90% 0.25 (0.52, 0.12)</td>
</tr>
<tr>
<td>Kilduff et al. (2004) (30)</td>
<td>39.25 0.4 11</td>
<td>39.5 0.55 10</td>
<td>6.30% 0.30 (0.65, 0.05)</td>
</tr>
<tr>
<td>Mendel et al. (2005) (41)</td>
<td>38.1 0.4 8</td>
<td>38.4 0.3 8</td>
<td>9.00% 0.18 (0.01, 0.35)</td>
</tr>
<tr>
<td>Volek et al. (2001) (56)</td>
<td>38.57 0.07 10</td>
<td>38.39 0.26 10</td>
<td>38.70% 0.10 (0.22, 0.42)</td>
</tr>
<tr>
<td>Watson et al. (2006) (57)</td>
<td>39.4 0.4 12</td>
<td>39.3 0.4 12</td>
<td>10.50% 0.10 (0.27, 0.31)</td>
</tr>
<tr>
<td>Weiss et al. (2006) (59)</td>
<td>38.44 0.42 12</td>
<td>38.42 0.29 12</td>
<td>12.9 0.03 (0.42, 0.48)</td>
</tr>
<tr>
<td>Wright et al. (2007) (61)</td>
<td>38.07 0.47 10</td>
<td>38.04 0.56 10</td>
<td>5.30% 0.03 (0.07, 0.13)</td>
</tr>
<tr>
<td>Overall</td>
<td>38.84 0.47 84</td>
<td>38.83 0.56 83</td>
<td>100.00% 0.03 (0.07, 0.13)</td>
</tr>
</tbody>
</table>

**Table 2.** Results of studies investigating the influence of caffeine on hydration status and exercise heat tolerance.*

Heterogeneity: \(X^2 = 10.90, df = 7, P = 0.14, I^2 = 36\%\). Test for overall effect \(Z = 0.56, P = 0.57\).


**Fixed-effects, inverse variance model.**
TABLE 3. Diuretic effect of caffeine, considering dose and volume of fluid consumed.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Gender, Protocol Duration (h), Scenario</th>
<th>Caffeine Dose (mg)</th>
<th>Did Caffeine Induce Significant\textsuperscript{b} Diuresis?</th>
<th>Volume of Fluid Consumed (mL)\textsuperscript{c}</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 women and 6 men, 24 h, in a laboratory</td>
<td>642</td>
<td>Yes at rest and sleep</td>
<td>3294</td>
<td>22</td>
</tr>
<tr>
<td>4 men and 2 women, 4 h, laboratory cycling</td>
<td>586</td>
<td>Yes at rest, no during exercise</td>
<td>2560</td>
<td>30</td>
</tr>
<tr>
<td>7 men, 62–64 min, treadmill walking with 22 kg load</td>
<td>553</td>
<td>No during exercise</td>
<td>200</td>
<td>11</td>
</tr>
<tr>
<td>19 men, 6 d, free–living</td>
<td>452\textsuperscript{d}</td>
<td>No during free–living and sleep</td>
<td>1821–2247d\textsuperscript{–1}</td>
<td>3</td>
</tr>
<tr>
<td>19 men, 16 h, post–EHT and free–living</td>
<td>452\textsuperscript{d}</td>
<td>No during daily activities and sleep</td>
<td>2600</td>
<td>8</td>
</tr>
<tr>
<td>8 men, 4 h, resting in laboratory</td>
<td>360\textsuperscript{d}</td>
<td>Yes at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
<tr>
<td>Male medical students, 4 h, at rest in laboratory</td>
<td>300</td>
<td>No at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
<tr>
<td>12 women, 3 h, resting in laboratory</td>
<td>300</td>
<td>No at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
<tr>
<td>15 men, 3 h, resting in laboratory</td>
<td>300</td>
<td>No at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
<tr>
<td>37 women, 2 h, resting in laboratory</td>
<td>274</td>
<td>No at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
<tr>
<td>18 men, free–living, 24 h</td>
<td>253\textsuperscript{d}</td>
<td>No during daily activities and sleep</td>
<td>2800</td>
<td>16</td>
</tr>
<tr>
<td>9 men, 3 h post–exercise rehydration, lying supine in laboratory</td>
<td>250</td>
<td>Yes at rest</td>
<td>300</td>
<td>26</td>
</tr>
<tr>
<td>16 men and 3 women, 2 h, post–exercise</td>
<td>250</td>
<td>Yes at rest</td>
<td>1958</td>
<td>14</td>
</tr>
<tr>
<td>7 women and 3 men, 4 h\textsuperscript{e} \textsuperscript{f} for 3 d, outdoor field sports</td>
<td>245</td>
<td>No during exercise and rest periods</td>
<td>3800–3967d\textsuperscript{–1}</td>
<td>12</td>
</tr>
<tr>
<td>12 men, 6 h, resting in laboratory</td>
<td>240</td>
<td>Yes at rest</td>
<td>750</td>
<td>25</td>
</tr>
<tr>
<td>20 men, 11 d, free–living</td>
<td>226\textsuperscript{d}</td>
<td>No during free–living and sleep</td>
<td>2078–2384d\textsuperscript{–1}</td>
<td>3</td>
</tr>
<tr>
<td>20 men, 16 h, post–EHT and free–living</td>
<td>226\textsuperscript{d}</td>
<td>No during daily activities and sleep</td>
<td>3280</td>
<td>8</td>
</tr>
<tr>
<td>8 men, 4 h, resting in laboratory</td>
<td>180\textsuperscript{d}</td>
<td>No at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
<tr>
<td>12 women, 3 h, resting in laboratory</td>
<td>150</td>
<td>No at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
<tr>
<td>15 men, 3 h, resting in laboratory</td>
<td>150</td>
<td>No at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
<tr>
<td>18 men, free–living, 24 h</td>
<td>114\textsuperscript{d}</td>
<td>No during daily activities and sleep</td>
<td>2800</td>
<td>16</td>
</tr>
<tr>
<td>8 men, 4 h, resting in laboratory</td>
<td>90\textsuperscript{d}</td>
<td>No at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
<tr>
<td>8 males, 4 h, resting in laboratory</td>
<td>45\textsuperscript{d}</td>
<td>No at rest</td>
<td>946–1419</td>
<td>24</td>
</tr>
</tbody>
</table>


\textsuperscript{b}Comparison of group mean values for caffeine vs water or placebo (P < 0.05) in controlled–randomized experiments.

\textsuperscript{c}Some studies reported only fluid intake, others total water intake from food + fluid.

\textsuperscript{d}Multiple caffeine doses (compare with same study in other rows).

\textsuperscript{e}Data not reported.

EHT = exercise–heat tolerance test (90 min treadmill walking, 37.7°C).

Results of the various studies examining the effects of caffeine on hydration status suggest that there is little evidence to support the recommendations for exercising individuals to avoid caffeine, particularly when exercising in the heat.

GLYCEROL

Compared with the other nutritional supplements mentioned in this review, glycerol is the only ergogenic supplement with purported beneficial effects on hydration status and/or heat tolerance (Table 1). Researchers have investigated various means of hyperhydrating athletes before exercise, particularly for endurance events where hydrating during exercise can be difficult. Hyperhydration with water alone has resulted in increased urine output soon after ingestion, thus leading to ineffective hyperhydration. As a result, several studies have investigated the effects of glycerol ingestion with water to promote hyperhydration to decrease cardiovascular and thermoregulatory strain and improve exercise performance (3,24,25,28,31,36,38,40,44,46,49,60). A metaanalysis on the effects of glycerol-induced hyperhydration on fluid retention and exercise performance revealed that hyperhydration with glycerol improved fluid retention by 50% compared to hyperhydration with water alone (24). Glycerol is a naturally occurring three-carbon molecule that increases the concentration of fluid in the blood and tissues (49). Increases in blood osmolality together with increased water intake would result in an osmotic drive resulting in water retention (49).

The available literature on the influence of glycerol on increasing athletic performance and/or improving various physiological responses is inconclusive. Various researchers have found that hyperhydration with glycerol has improved performance significantly versus hyperhydration with water alone (25,28,44). However, others have found no significant
differences in exercise performance when subjects were hyperhydrated with glycerol (28,36,38,60). Data regarding the influence of glycerol on cardiovascular, thermoregulatory, and other physiologic responses also have varied. While some studies have found decreases in cardiovascular and/or thermoregulatory strain with glycerol ingestion (25,28,38,44,46,60), others have found no significant differences between glycerol and placebo (31,38).

Studies investigating the effects of glycerol ingestion before exercise in the heat also varied in the results; however, overall there were no definite advantages to glycerol over water in three out of these four studies (3,28,38,60). Anderson et al. found that glycerol ingestion prior to 90 min of steady-state cycling resulted in fluid retention that was capable of reducing cardiovascular strain and enhancing thermoregulation (3). Similarly, Kavouras et al.’s findings in a rehydration study suggest that glycerol ingestion prior to cycling in the heat improved exercise capacity (28). Subjects exercised 19% and 72% longer in the glycerol trial versus both the water only and the non-fluid trials, respectively. However, despite increased cutaneous vascular conductance and improved exercise capacity attributed to plasma volume expansion, there were no significant differences in urine output or other cardiovascular measures with glycerol compared with water or no fluid conditions (28).

In contrast to Anderson et al.’s findings, Marino et al. found no significant improvements in exercise performance with glycerol ingestion (38). Despite increases in sweat rate and urine osmolality in the glycerol condition compared with placebo, a 60-min self-paced cycling bout in 34.5°C resulted in no decrease in thermoregulatory strain or increased performance. An investigation on the effects of pre-exercise glycerol on performance and physiological function during a mountain bike race in the heat found that glycerol with water did not affect cardiovascular or thermoregulatory responses compared with hydration without glycerol, despite decreased urine output and water retention found with glycerol (60). Researchers also examined the effects of glycerol ingestion for both hyperhydration and as a rehydrating agent following 120 min of exercise-induced dehydration. Results indicated the glycerol trial had significantly greater fluid retention (approximately 700 mL) compared with placebo (36).

The varying results in the literature could be attributed to differences in methodology, such as the time between glycerol hyperhydration and exercise. Studies with a greater gap between hyperhydration and exercise, such as 3 h post-glycerol, found approximately 600 mL greater total body water (34). Moreover, when subjects were hyperhydrated pre-exercise and rehydrated during exercise, the hydration advantages of glycerol over water alone were lost. Similarly, when exercise start time was within 1 h of hyperhydration, there were no differences in hydration status between glycerol and water (34). Differences in exercise and hydration protocols also have been inconclusive. Therefore, the variability in the literature makes it difficult to elucidate whether hyperhydration with glycerol improves thermoregulation or decreases cardiovascular strain during exercise, particularly while exercising in the heat. However, in certain situations (such as the inability to consume large amounts of fluid during intense exercise in the heat or not having access to fluids), the use of preexercise glycerol may assist with maintaining hydration status during exercise.

**Ephedra**

The use of the supplement ephedra, from the Chinese plant species ma huang, has been controversial in the last decade. Although the use of ephedra dates back more than 5000 yr (1), only recently has the supplement been exposed as a potential performance enhancer and weight loss aid. Recent high-profile athlete deaths have been linked to the use of supplements such as ephedrine (7,15). Ephedrine is the major isomer making up 30% to 90% of the total alkaloids found in ephedra (1); the other ephedra alkaloids include pseudoephedrine, norpseudoephedrine, and methyl-ephedrine (2). Ephedra, often in combination with caffeine, has been associated with possibly predisposing athletes to exertional heat stroke, particularly with individuals exercising in hot, humid environments (15,33).

As a result of speculations that ephedra is to blame for some of these high-profile deaths, several sports organizations have banned the use of ephedra for athletes. Several consumer health groups requested that the U.S. Food and Drug Administration (FDA) ban the sale of ephedra-containing products, despite the lack of scientific evidence linking ephedrine to these reported deaths or serious side effects. Dietary supplements are regulated by the Dietary Supplement Health and Education Act of 1994 (DSHEA); the FDA can only ban a supplement if there is sufficient convincing evidence that the product is harmful (53). A review of 52 randomized controlled trials investigating the effects of ephedra-containing dietary supplements on weight loss and/or athletic performance found there were no serious adverse events, such as death or cardiovascular events; however, some of the side effects reported included anxiety, autonomic hyperactivity, palpitations, and headache (53). It could be theorized that increases in heart rate and metabolic rate as a result of ephedra may lead to an increased heat load or some impairment in the body’s ability to dissipate heat at the same rate that it is being generated. However, there has been no evidence of elevated core body temperature or heat intolerance in these randomized controlled trials (Table 1). The subjects used in these clinical trials, however, were healthy and had been screened for predisposing factors to illness.

There is a paucity of data regarding the potential influence of ephedra-containing supplements on thermoregulation. Several studies have investigated the effects of ephedrine with caffeine (8–11,37), since many products on the market contain both of these ingredients. However, many of these studies were examining the influence of ephedrine on exercise performance and did not report thermoregulatory measures (8,10,11,45). One study by Bell and associates examined the effects of caffeine and ephedrine (C+E) ingestion on thermal regulation during heat stress trials in 40°C (9). Initial pre-exercise rectal temperatures ($T_{re}$) were not different, and changes in $T_{re}$ throughout the exercise bouts were not significantly different between C+E and placebo conditions (9).
There have, however, been several case studies linking ephedra to exertional heat stroke (15,47). The death of the Baltimore Orioles’ pitcher Steve Bechler was linked initially to ephedrine supplements that he was taking when he collapsed from exertional heat stroke (15). However, it has been suggested that there were several other factors in Bechler’s case that may have either predisposed him to heat stroke (e.g., history of heat illness, lack of acclimatization, and several layers of clothing) or contributed to his death (improper treatment). Therefore, ephedrine could not be solely responsible for his death (33).

Another case, of a highly trained infantry soldier, may be the only case, to our knowledge, to report a concrete connection between ephedra and exertional heat stroke (47). Although the mechanism through which ephedra may cause exertional heat stroke is not immediately clear, it is believed that ephedra may activate dopamine receptors and impair heat dissipation through vasoconstriction, thus producing a thermogenic effect (45). To date, there is insufficient evidence that ephedra can impair thermoregulation; however, the inability to conduct randomized controlled trials because of its potential negative effects may leave the effects of ephedra while exercising in the heat unknown. Furthermore, there have been sufficient case reports of deaths linked to ephedra (whether heat-related or not) to make one wary of suggesting ephedra as a safe supplement for athletes or other exercising individuals.

OTHER SUPPLEMENTS

With the abundance of supplements in the sports market and the lack of regulation by the FDA, it is not surprising that there are many unknowns regarding the effects of other supplements on hydration and thermoregulation. There are a few other supplements that can be used as ergogenic aids and warrant mention in this review with regard to their effect on hydration and/or thermoregulation. Although many studies have investigated the effects of branched-chain amino acids (BCAA) on exercise performance, few have examined the effect that BCAA supplementation may have on hydration status and/or thermoregulation. Cheuvront et al. examined the impact of BCAA supplementation and performance in the heat when hypohydrated (16). This study found that exercise in the heat (40°C) after ingestion of either an isocaloric BCAA and carbohydrate drink or a carbohydrate-only drink resulted in no differences in core body temperature. Similarly, Mittleman et al. compared the effects of a BCAA drink to a placebo during exercise in the heat (34.4°C) and found no significant differences in core body temperature or sweat losses (43). In a study comparing the effects of varying levels of protein intake on hydration indexes, Martin et al. found that although plasma osmolality and urine specific gravity were elevated as protein intake increased, these hydration indexes were still within normal limits (39). Therefore, the effect of increased protein intake on measures of hydration status was minimal.

The combination of several dietary supplements was also believed to have caused a malignant hyperthermia reaction in an otherwise healthy trauma patient (13). A 24-yr-old male trauma patient developed malignant hyperthermia after receiving the anesthetic sevoflurane in the operating room. The family denied a history of malignant hyperthermia and heat/exercise intolerance; however, upon recovery the patient admitted to 6 months of daily intense exercise, ingestion of creatine monophosphate and Ripped Fuel® (containing caffeine, ephedrine, and aspirin), daily injections of deca-durabolin (an anabolic steroid), and weekly testosterone (13). Although the authors of this case study had several hypotheses for the occurrence of malignant hyperthermia, the most prominent conclusion was that the patient may have increased intracellular calcium pharmacologically and altered skeletal muscle metabolism, which combined with the anesthetic may have contributed to the rapid malignant hyperthermia. Although the use of these supplements could not be confirmed as the cause of the hyperthermia, this case study epitomizes the idea that the effects of combining uncontrolled supplements may be deleterious.

The effects of some prescribed medications on hydration status and/or thermoregulation also warrant more randomized controlled trials, particularly when combined with exercise in the heat. Recent studies on the effects of acute dopamine reuptake inhibition have demonstrated elevated temperatures during an exercise bout in the heat (50,58). Ingestion of methylphenidate, a medication commonly prescribed to children and adults for the treatment of attention deficit hyperactivity disorder (ADHD) resulted in increased exercise performance as well as increased core temperatures only in the warm condition (30°C) compared to a temperate condition (18°C) (50). The subjects’ perceptual responses of ratings of perceived exertion and thermal stress were not influenced by the drug treatment (50). This could be potentially dangerous during intense exercise in the heat, as athletes taking this medication may be susceptible to higher body temperatures while signals from the central nervous system to decrease intensity or cease exercise may be inhibited.

CONCLUSION

Exercising in the heat can predispose an athlete to an exertional heat illness if preventative measures are not heeded. Given that supplements are easily available and the veracity of their contents are tainted, it is imperative to remain abreast of the most recent evidence regarding supplementation to better educate and advise athletes. One also must rely on empirical evidence when making conclusions about the efficacy of a supplement while not ignoring significant anecdotal reports that more closely may resemble real-life situations. There continues to be an immense need for more randomized, controlled trials on the influence of nutritional supplements on hydration and thermoregulation in order to determine their clinical application in the sports arena.

References